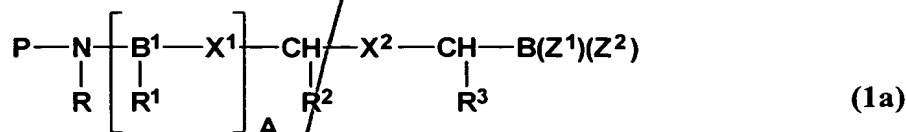


What Is Claimed Is:

1. A compound having the formula:



and pharmaceutically acceptable salts thereof;

wherein

P is $\text{R}^7-\text{C}(\text{O})-$ or R^7-SO_2- , where R^7 is one of aryl, aralkyl, heteroaryl or heteroarylalkyl, the ring portion of any of which can be optionally substituted, or when P is $\text{R}^7-\text{C}(\text{O})-$, R^7 can also be N-morpholinyl;

B^1 , at each occurrence, is independently one of N or CH;

X^1 , at each occurrence, is independently one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}_2-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{CH}(\text{OH})-\text{CH}_2-\text{NH}-$, $-\text{CH}=\text{CH}-$, $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$, provided that when B^1 is N, then the X^1 attached to said B^1 is $-\text{C}(\text{O})-\text{NH}-$;

X^2 is one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$;

R is hydrogen or alkyl, or R forms together with the adjacent R^1 , or when A is zero, forms together with the adjacent R^2 , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R^1 , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{CH}_2-\text{R}^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R² is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

~~A is 0, 1, or 2.~~

2. The compound of claim 1, wherein:

A is zero;

X is -C(O)-NH-;

R is hydrogen or C₁₋₈alkyl; and

R₃ is C₁₋₆alkyl.

3. The compound of claim 2, wherein R₃ is C₄alkyl.

4. The compound of claim 1, wherein:

P is R⁷-C(O)- or R⁷-SO₂-, where R⁷ is one of quinolinyl, quinoxalinyl, pyridyl, pyrazinyl, furanyl or pyrrolyl, or when P is R⁷-C(O)-, R⁷ can also be N-morpholinyl.

5. The compound of claim 1, wherein P is one of quinolinecarbonyl, pyridinecarbonyl, quinolinesulfonyl, quinoxalinecarbonyl, quinoxalinesulfonyl, pyrazinecarbonyl, pyrazinesulfonyl, furancarbonyl, furansulfonyl or N-morpholinylcarbonyl.

6. The compound of claim 5, wherein P is one of 8-quinolinecarbonyl, 8-quinolinesulfonyl, 2-quinoxalinecarbonyl, 2-quinoxalinesulfonyl, 2-pyrazinecarbonyl, 2-pyrazinesulfonyl, 3-furancarbonyl, 3-furansulfonyl or N-morpholinecarbonyl.

7. The compound of claim 1, wherein A is O.

8. The compound of claim 1, wherein B¹, at each occurrence, is CH.

9. The compound of claim 8, wherein X¹, at each occurrence, is -C(O)-NH-.

~~10. The compound of claim 9, wherein X² is -C(O)-NH-.~~

11. The compound of claim 1, wherein R is hydrogen or C₁₋₈ alkyl.

12. The compound of claim 1, wherein:
R¹, at each occurrence, and R² and R³ are each independently one of hydrogen, C₁₋₈ alkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, a 5-, 6-, 9- or 10- membered heteroaryl group, or -CH₂-R⁵;

R⁵, in each instance, is one of C₆₋₁₀ aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, C₁₋₆ alk(C₆₋₁₀)aryl, C₃₋₁₀ cycloalkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio or a 5-, 6-, 9- or 10- membered heteroaryl group;

where the ring portion of any of said aryl, aralkyl, alkaryl or 5-, 6-, 9- or 10- membered heteroaryl groups of R¹, R², R³ and R⁵ can be optionally

substituted by one or two substituents independently selected from the group consisting of C₁₋₆alkyl, C₃₋₈cycloalkyl, C₁₋₆alkyl(C₃₋₈)cycloalkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cyano, amino, C₁₋₆alkylamino, di(C₁₋₆)alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C₁₋₆)alkoxy, trifluoromethyl, halogen, C₁₋₆alkoxy, C₆₋₁₀aryl, C₆₋₁₀aryl(C₁₋₆)alkyl, C₆₋₁₀aryl(C₁₋₆)alkoxy, hydroxy, C₁₋₆alkylthio, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₆₋₁₀arylthio, C₆₋₁₀arylsulfinyl, C₆₋₁₀arylsulfonyl, C₆₋₁₀aryl, C₁₋₆alkyl(C₆₋₁₀)aryl, and halo(C₆₋₁₀)aryl.

13. The compound of claim 1, wherein R₃ is C₁₋₁₂alkyl.

14. The compound of claim 1, wherein R₃ is C₁₋₆alkyl.

15. The compound of claim 1, wherein R₃ is C₄alkyl.

16. The compound of claim 1, wherein R³ is isobutyl.

17. The compound of claim 1, wherein R² is one of isobutyl, 1-naphthylmethyl, 2-naphthylmethyl, 3-pyridylmethyl, 2-pyridylmethyl, 6-quinolinylmethyl, 3-indolylmethyl, benzyl, 4-fluorobenzyl, 4-hydroxybenzyl, 4-(2'-pyridylmethoxy)benzyl, 4-(benzyloxy)benzyl, benzylnaphthylmethyl or phenethyl.

18. The compound of claim 1, wherein Z¹ and Z² are independently one of C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy.

19. The compound of claim 1, wherein Z¹ and Z² are both hydroxy.

20. The compound of claim 1, wherein together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting

of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

15
21. The compound of claim 1, wherein:

P is one of quinolinecarbonyl, pyridinecarbonyl, quinolinesulfonyl, quinoxalinecarbonyl, quinoxalinesulfonyl, pyrazinecarbonyl, pyrazinesulfonyl, furancarbonyl, furansulfonyl or N-morpholinylcarbonyl;

A is zero;

X² is -C(O)-NH-;

R is hydrogen or C₁₋₈ alkyl;

10 R² and R³ are each independently one of hydrogen, C₁₋₈alkyl, C₃₋₁₀cycloalkyl, C₆₋₁₀aryl, C₆₋₁₀ar(C₁₋₆)alkyl, pyridylmethyl, or quinolinylmethyl; and

15 Z¹ and Z² are both hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

22. The compound of claim 1, wherein:

20 P is one of 8-quinolinecarbonyl, 8-quinolinesulfonyl, 2-quinoxalinecarbonyl, 2-quinoxalinesulfonyl, 2-pyrazinecarbonyl, 2-pyrazinesulfonyl, 3-pyridinecarbonyl, 3-pyridinesulfonyl, 3-furancarbonyl, 3-furansulfonyl or N-morpholinecarbonyl;

A is zero;

X² is -C(O)-NH-;

25 R is hydrogen or C₁₋₈ alkyl;

R³ is isobutyl;

R² is one of isobutyl, 1-naphthylmethyl, 2-naphthylmethyl, 3-pyridylmethyl, 2-pyridylmethyl 6-quinolinylmethyl, 3-indolylmethyl, benzyl,

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4-fluorobenzyl, 4-hydroxybenzyl, 4-(2'-pyridylmethoxy)benzyl, 4-(benzyloxy)benzyl, benzylnaphthylmethyl or phenethyl; and

Z^1 and Z^2 are independently one of hydroxy, C_{1-6} alkoxy, C_{6-10} aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

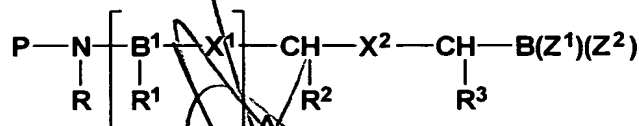
23. The compound of claim 1, wherein said compound is one of:

N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,
N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(8-quinoline)sulfonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid;

or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

24. The compound of claim 23, wherein said compound is *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid, or an isostere, pharmaceutically acceptable salt or boronate ester thereof.

25. A compound having the formula:



(1a)

wherein

P is hydrogen or an amino-group-protecting moiety;

B¹, at each occurrence, is independently one of N or CH;

X¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-,
5 -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-,
-C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided
that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

X² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-,
10 -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R is hydrogen or alkyl, or R forms together with the adjacent R¹, or when
A is zero, forms together with the adjacent R², a nitrogen-containing mono-, bi-
or tri-cyclic, saturated or partially saturated ring system having 4-14 ring
members, that can be optionally substituted by one or two of keto, hydroxy, aryl,
alkoxy or aryloxy;

15 R¹ at each occurrence, R² and R³ are each independently one of hydrogen,
alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or
aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl,
aralkyl, alkaryl or heterocycle can be optionally substituted;

20 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a
5-10 membered saturated, partially unsaturated or aromatic
heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl,
where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

25 provided that at least one R¹, R² or R³ is naphthylmethyl,
pyridylmethyl or quinolinylmethyl;

30 Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or
together Z¹ and Z² form a moiety derived from a dihydroxy compound having at
least two hydroxy groups separated by at least two connecting atoms in a chain
or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom
or heteroatoms which can be N, S, or O; and

or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2;

provided that the compound is other than isovaleryl-phenylalanine-norvaline-[(naphthylmethyl), (4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)]methanamide or (3-t-butylsulfonyl)propionyl-norvaline-(1-naphthyl, dihydroxyboryl)methanamide.

26. The compound of claim 25, wherein P is $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be saturated or partially saturated heterocycle.

27. The compound of claim 25, wherein P is $R^7-C(O)-$ or R^7-SO_2- ; and

R^7 is one of C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, 5- to 10-membered heteroaryl or 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

28. The compound of claim 25, wherein B^1 is CH, and X^1 and X^2 are each $-C(O)-NH-$.

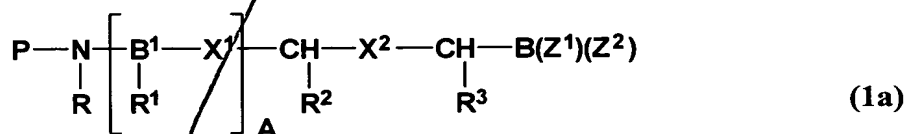
29. The compound of claim 25, wherein R^1 and R^2 are independently selected from the group consisting of alkyl and $-CH_2-R^5$, where R^5 is one of C_{6-10} aryl, C_{1-10} alkyl(C_{6-10})aryl, C_{3-10} cycloalkyl, or a 5-, 6-, 9- or 10-membered heterocycle.

30. The compound of claim 25, wherein A is zero.

31. The compound of claim 25, wherein R² is quinolinylmethyl.

32. The compound of claim 25, wherein said compound is one of:
N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid, or
N-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid;
 or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

33. A compound having the formula:



and pharmaceutically acceptable salts thereof;
 wherein

P is hydrogen or an amino-group-protecting moiety;

B¹, at each occurrence, is independently one of N or CH;

X¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-,
 -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-,
 -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided
 that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

X² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-,
 -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R forms together with the adjacent R¹, or when A is zero, forms together
 with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or
 partially saturated ring system having 4-14 ring members, and one or two
 optional substituents selected from the group consisting of keto, hydroxy, alkyl,
 aryl, aralkyl, alkoxy and aryloxy;

when A is 2, the R¹ that is not adjacent to N-R is one of hydrogen, alkyl,
 cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic
 heterocycle or -CH₂-R⁵;

when A is 1 or 2, R² is one of hydrogen, alkyl, cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵;

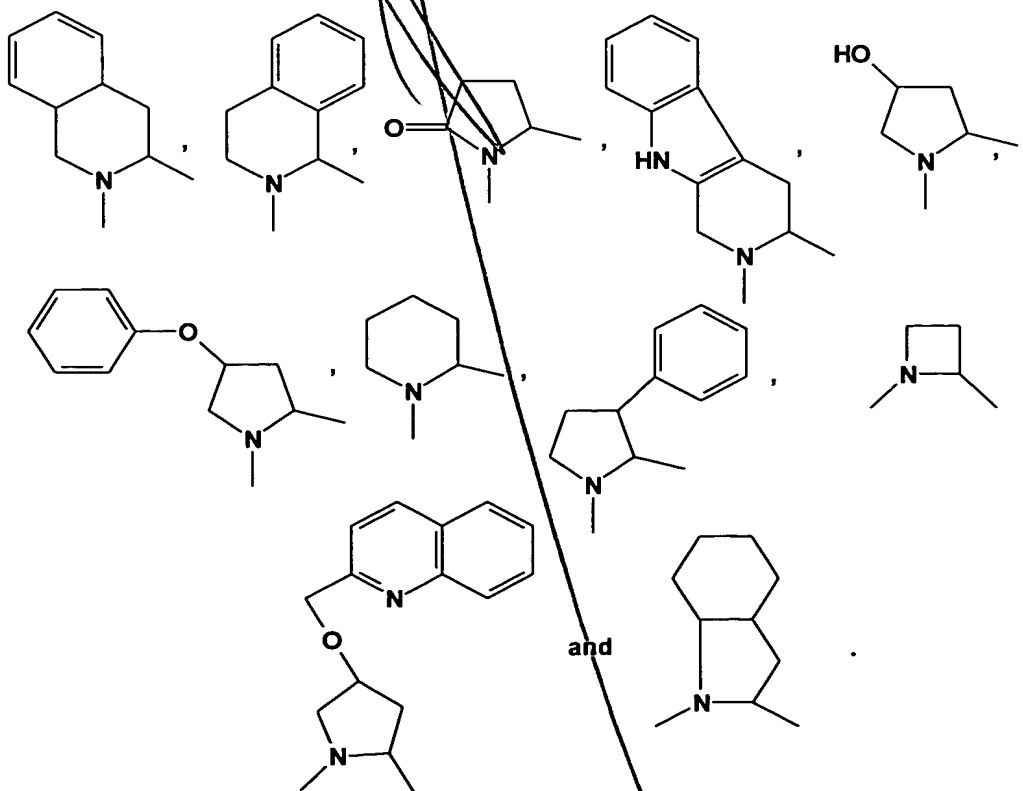
R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵;

5 R⁵, in each instance, is independently one of aryl, aralkyl, alkaryl, cycloalkyl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl;

10 Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2.

15 34. The compound of claim 33, wherein the nitrogen-containing ring system is selected from the group consisting of:



35. The compound of claim 33, wherein P is $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be saturated or partially saturated heterocycle.

36. The compound of claim 35, wherein P is $R^7-C(O)-$ or R^7-SO_2- ; and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, 5- to 10-membered heteroaryl or 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

37. The compound of claim 33, wherein B^1 is CH, and X^1 and X^2 are each $-C(O)-NH-$.

38. The compound of claim 33, wherein R^1 and R^2 are independently selected from the group consisting of alkyl and $-CH_2-R^5$, where

R^5 , in each instance, is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, C_{1-6} alk(C_{6-10})aryl, C_{3-10} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio or a 5-, 6-, 9- or 10-membered heteroaryl group, where the ring portion of any of said C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, C_{1-6} alk(C_{6-10})aryl, or 5-, 6-, 9- or 10- membered heteroaryl can be optionally substituted by one or two substituents independently selected from the group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl(C_{3-8})cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, cyano, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C_{1-6})alkoxy, trifluoromethyl, halogen, C_{1-6} alkoxy, C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, C_{6-10} aryl(C_{1-6})alkoxy, hydroxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{6-10} arylthio, C_{6-10} arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} aryl, C_{1-6} alkyl(C_{6-10})aryl and halo(C_{6-10})aryl.

39. The compound of claim 33, wherein A is zero.

40. The compound of claim 33, wherein P is hydrogen.

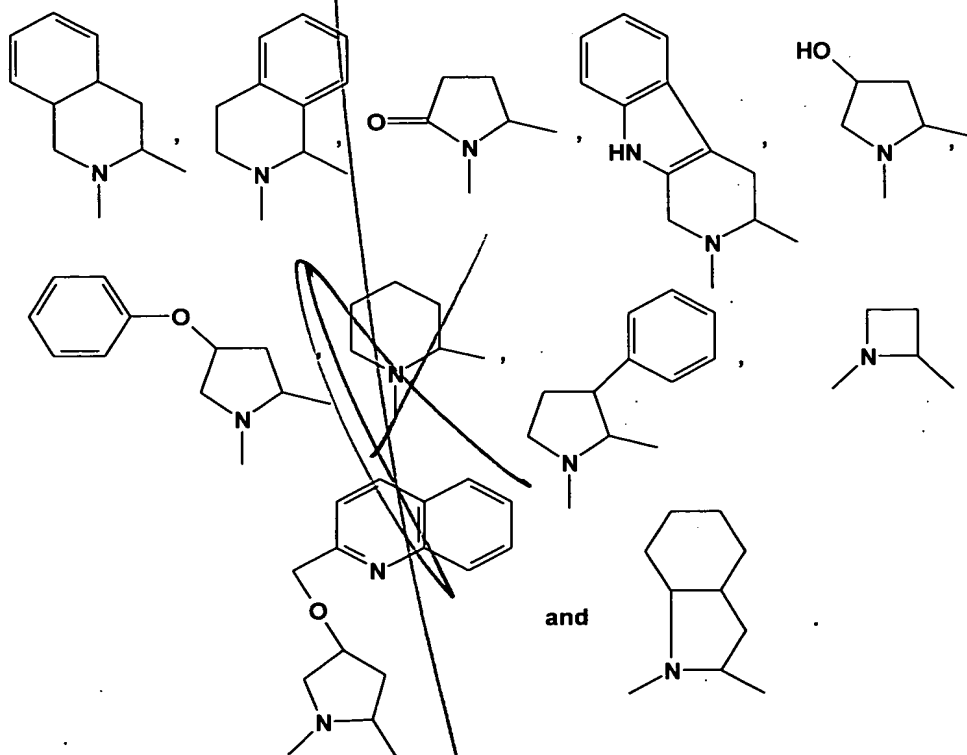
41. The compound of claim 33, wherein:

A is zero;

P is hydrogen;

X² is -C(O)-NH-

R forms together with the adjacent R², a nitrogen-containing ring system selected from the group consisting of:



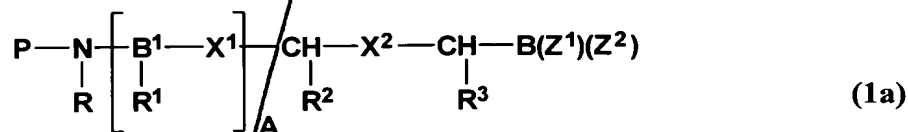
R³ is C₁₋₆alkyl; and

Z¹ and Z² are both hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene

glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

42. The compound of claim 33, wherein said compound is L-proline-L-leucine boronic acid, or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

43. A compound having the formula:



and pharmaceutically acceptable salts thereof;
wherein

P is hydrogen or an amino-group-protecting moiety;

B¹, at each occurrence, is independently one of N or CH;

X¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

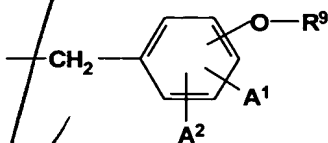
X² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R is hydrogen or alkyl, or R forms together with the adjacent R¹, or when A is zero, forms together with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, and one or two optional substituents selected from the group consisting of keto, hydroxy, aryl, alkoxy and aryloxy;

R¹ at each occurrence, R² and R³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or

aromatic heterocycle or $-\text{CH}_2-\text{R}^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R^5 , in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{W}-\text{R}^6$, where W is a chalcogen and R^6 is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted, provided that at least one R^1 , R^2 or R^3 is



where R^9 is one of hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or heteroarylalkyl; wherein the alkyl is optionally substituted with one of C_{1-6} alkyl, halogen monohalo(C_{1-6})alkyl and trifluoromethyl; and wherein said cycloalkyl, aryl, aralkyl, heteroaryl and heteroarylalkyl groups can be optionally substituted with one or two of C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl(C_{3-8})cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, cyano, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C_{1-6})alkoxy, trifluoromethyl, halogen, C_{1-6} alkoxy, C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, C_{6-10} aryl(C_{1-6})alkoxy, hydroxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{6-10} arylthio, C_{6-10} arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} aryl, C_{1-6} alkyl(C_{6-10})aryl, and halo(C_{6-10})aryl;

A^1 and A^2 are independently one of hydrogen, halogen, C_{1-6} alkyl, monohalo(C_{1-6})alkyl, or trifluoromethyl;

Z^1 and Z^2 are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain

or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2.

44. The compound of claim 43, wherein P is $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

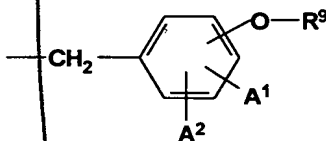
R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be saturated or partially saturated heterocycle.

45. The compound of claim 43, wherein P is $R^7-C(O)-$ or R^7-SO_2- ; and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, 5- to 10-membered heteroaryl or 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

46. The compound of claim 43, wherein X^1 and X^2 are each $-C(O)-NH-$.

47. The compound of claim 43, wherein one of R^1 , R^2 or R^3 is



where

A^1 and A^2 are independently one of hydrogen, C_{1-6} alkyl, halogen, monohalo (C_{1-6}) alkyl or trifluoromethyl;

R^9 is one of C_{1-8} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, a 5- to 10-membered heteroaryl or a 5- to 10-membered heteroaryl(C_{1-6})alkyl;

and the remaining R^1 , R^2 and R^3 are independently selected from the group consisting of alkyl and $-\text{CH}_2-\text{R}^5$, where

R^5 , in each instance, is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, C_{1-6} alk(C_{6-10})aryl, C_{3-10} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio or a 5-, 6-, 9- or 10-membered heteroaryl group, where the ring portion of any of said C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, C_{1-6} alk(C_{6-10})aryl, or 5-, 6-, 9- or 10- membered heteroaryl can be optionally substituted by one of two substituents independently selected from the group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl(C_{3-8})cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, cyano, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C_{1-6})alkoxy, trifluoromethyl, halogen, C_{1-6} alkoxy, C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, C_{6-10} aryl(C_{1-6})alkoxy, hydroxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{6-10} arylthio, C_{6-10} arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} aryl, C_{1-6} alkyl(C_{6-10})aryl and halo(C_{6-10})aryl.

48. The compound of claim 43, wherein A is zero.

49. The compound of claim 43, wherein:

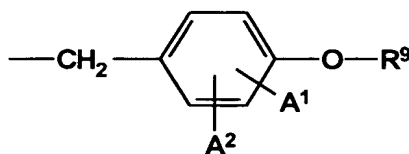
A is zero;

P is one of $\text{R}^7-\text{C}(\text{O})-$, R^7-SO_2- , $\text{R}^7-\text{NH}-\text{C}(\text{O})-$ or $\text{R}^7-\text{O}-\text{C}(\text{O})-$;

R^7 is one of quinolinyl, quinoxaliny, pyridyl, pyrazinyl, furanyl or pyrrolyl, or when P is $\text{R}^7-\text{C}(\text{O})-$, R^7 can also be N-morpholinyl;

X^2 is $-\text{C}(\text{O})-\text{NH}-$;

R^2 is:



where

A^1 and A^2 are independently one of hydrogen, C_{1-6} alkyl, halogen, monohalo (C_{1-6}) alkyl or trifluoromethyl;

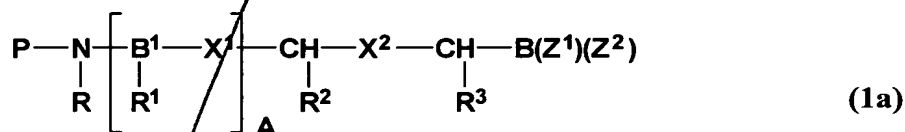
R⁹ is one of hydrogen, C₁₋₈alkyl, phenyl, benzyl, phenethyl or pyridylmethyl;

R³ is C₁₋₆alkyl; and

Z¹ and Z² are both hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

50. The compound of claim 43, wherein said compound is one of:
N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or
 isosteres, pharmaceutically acceptable salts or boronate esters thereof.

51. A compound having the formula:



and pharmaceutically acceptable salts thereof;

wherein

A is zero;

P is hydrogen or an amino-group-protecting moiety;

X² is one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-,
 -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-,
 -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R is hydrogen or alkyl, or R forms together with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring

system having 4-14 ring members, where said ring system can be optionally substituted by one or two of keto, hydroxy, aryl, alkoxy or aryloxy;

R^2 and R^3 are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R^5 , in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-W-R^6$, where W is a chalcogen and R^6 is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

Z^1 and Z^2 are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O;

provided that P is not C_{1-6} alkoxycarbonyl, C_{1-4} alkylcarbonyl or phenyl(C_{1-3})alkyl.

52. The compound of claim 51, wherein P is $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, where the ring portion of any of said aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be a saturated or partially unsaturated heterocycle.

53. The compound of claim 51, wherein P is $R^7-C(O)-$ or R^7-SO_2- ; and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, a 5- to 10-membered heteroaryl or a 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

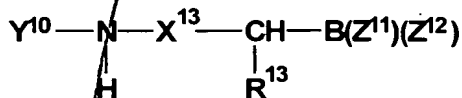
54. The compound of claim 51, wherein B^1 is CH, and X^1 and X^2 are each $-C(O)-NH-$.

55. The compound of claim 51, wherein R^2 and R^3 are independently selected from the group consisting of C_{1-8} alkyl and $-CH_2-R^5$, where R^5 is one of C_{6-10} aryl, C_{1-6} alk(C_{6-10})aryl, C_{6-10} ar(C_{1-6})alkyl, C_{3-8} cycloalkyl, or a 5-, 6-, 9- or 10-membered heterocycle.

56. The compound of claim 51, which is *N*-(3-phenylpropionyl)-L-phenylalanine-L-leucine boronic acid, or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

57. The compound of claim 51, wherein said compound is one of:
N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,
N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(8-quinoline)sulfonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or
isosteres, pharmaceutically acceptable salts or boronate esters thereof.

58. A compound having the formula:



(2a)

and pharmaceutically acceptable salts thereof;

wherein

Y is one of $\text{R}^8-\text{C}(\text{O})-$, R^8-SO_2- , $\text{R}^8-\text{NH}-\text{C}(\text{O})-$ or $\text{R}^8-\text{O}-\text{C}(\text{O})-$, where R^8 is one of alkyl, aryl, alkaryl, aralkyl, any of which can be optionally substituted, or when Y is $\text{R}^8-\text{C}(\text{O})-$ or R^8-SO_2- , then R^8 can also be an optionally substituted 5-10 membered, saturated, partially unsaturated or aromatic heterocycle;

X^3 is a covalent bond or $-\text{C}(\text{O})-\text{CH}_2-$;

R^3 is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{CH}_2-\text{R}^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R^5 , in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{W}-\text{R}^6$, where W is a chalcogen and R^6 is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

Z^1 and Z^2 are independently alkyl, hydroxy, alkoxy, aryloxy, or together form a moiety derived from dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O;

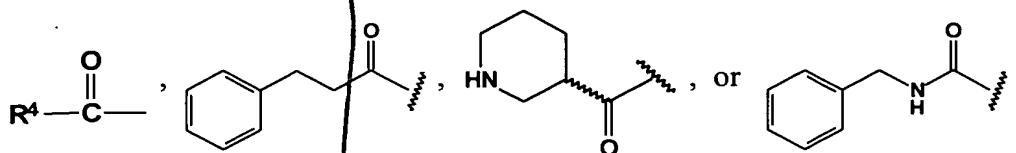
provided that when Y is $\text{R}^8-\text{C}(\text{O})-$, R^8 is other than phenyl, benzyl or C_{1-3} alkyl.

59. The compound of claim 58, wherein P is $\text{R}^8-\text{C}(\text{O})-$ or R^8-SO_2- ;

and

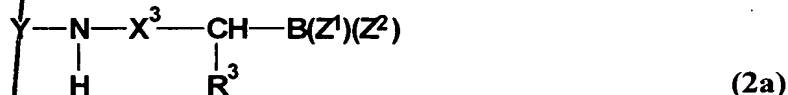
R^8 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, or a 5-10 membered heteroaryl, any of which can be optionally substituted, or when P is $R^8-C(O)-$, R^8 can also be N-morpholinyl.

60. The compound according to claim 58, wherein Y is one of



where R^4 is C_{6-12} alkyl.

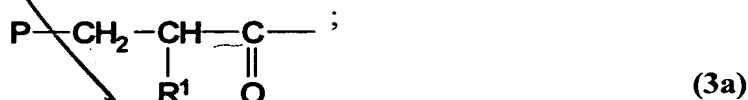
61. A compound having the formula:



and pharmaceutically acceptable salts thereof;

where

Y is



P is one of $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, where R^7 is one of alkyl, aryl, alkaryl, aralkyl, any of which can be optionally substituted, or when Y is $R^7-C(O)-$ or R^7-SO_2- , R^7 can also be an optionally substituted 5-10 membered saturated, partially unsaturated or aromatic heterocycle;

X^3 is a covalent bond or $-C(O)-CH_2-$;

R^1 , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

15

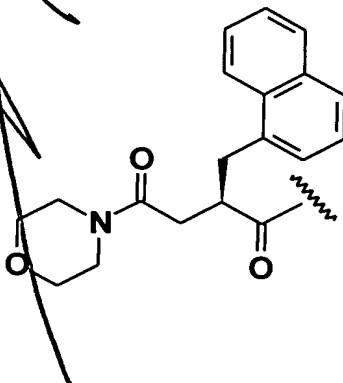
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R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

Z¹ and Z² are independently alkyl, hydroxy, alkoxy, aryloxy, or together form a moiety derived from dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O.

62. The compound of claim 61, wherein Y is:



63. A pharmaceutical composition, comprising a compound of claims 1, 25, 33, 43, 51, 58 or 61, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

64. A pharmaceutical composition, comprising a compound of claims 22, 28, 41, 49, 55, 60 and 62, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.



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R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R^{11} , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

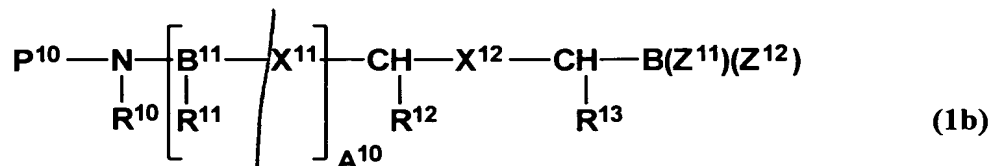
R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or $-chalcogen-alkyl$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A^{10} is 0, 1, or 2

69. A method for reducing the activity of NF- κ B in a cell, comprising contacting a cell in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X¹¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided that when B¹¹ is N, then X¹¹ is -C(O)-NH;

X¹² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

~~R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;~~

R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

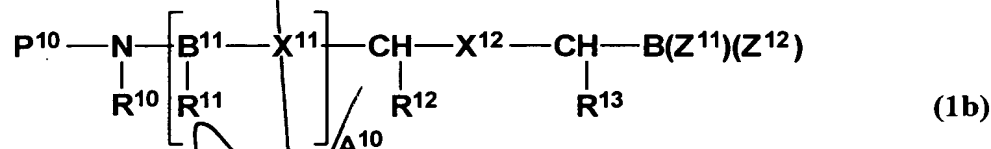
where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or

—chalcogen—alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A^{10} is 0, 1, or 2.

70. A method for reducing the rate of intracellular protein breakdown, comprising contacting cells in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^{11} is N, then X^{11} is $-C(O)-NH-$;

X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14

ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

5 R^{11} , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

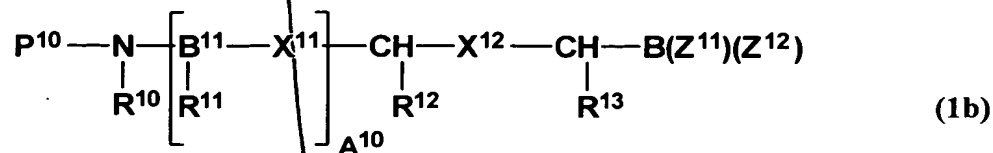
10 R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or $-chalcogen-alkyl$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

15 Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

20 A^{10} is 0, 1, or 2.

71. A method for reducing the rate of degradation of p53 protein in a cell, comprising administering to a cell in need of said reducing an effective amount of a proteasome inhibitor of the formula:



25 or a pharmaceutically acceptable salt thereof;
wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

X¹¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-,
-CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH-NH₂-, -CH=CH-,
5 -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided
that when B¹¹ is N, then X¹¹ is -C(O)-NH;

X¹² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-,
-C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or
10 when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing
mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14
ring members, that can be optionally substituted by one or two of keto, hydroxy,
alkyl, aryl, aralkyl, alkoxy or aryloxy;

R¹¹, at each occurrence, is independently one of hydrogen, alkyl,
15 cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic
heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl,
alkaryl or heterocycle can be optionally substituted;

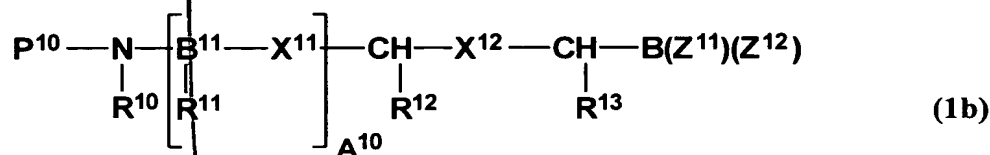
R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl,
aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or
20 -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered
saturated, partially unsaturated or aromatic heterocycle, or
-chalcogen-alkyl, where the ring portion of any of said aryl,
25 aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and
Z¹² together form a dihydroxy compound having at least two hydroxy groups
separated by at least two connecting atoms in a chain or ring, said chain or ring
comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can
30 be N, S, or O; and

A¹⁰ is 0, 1, or 2.

72. A method for inhibiting cyclin degradation in a cell, comprising contacting a cell in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

X¹¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided that when B¹¹ is N, then X¹¹ is -C(O)-NH;

X¹² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or

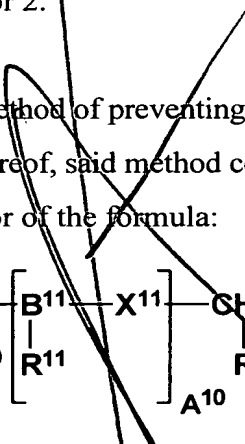
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 r of the formula:

$$\left[\begin{array}{c} \text{B}^{11} \\ | \\ \text{R}^{11} \end{array} - \text{X}^{11} - \text{CH} \right]_{\text{A}^{10}} \begin{array}{c} | \\ \text{F} \end{array}$$

15



wherein

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X¹² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

5 R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R^{11} , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

10 R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

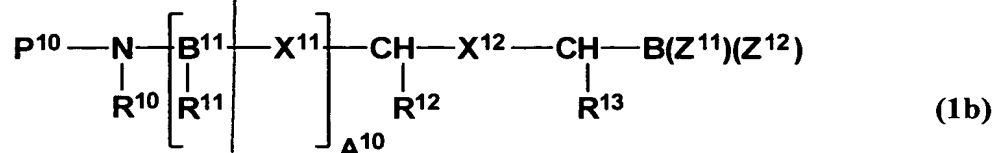
15 where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

20 Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A^{10} is 0, 1, or 2.

25 74. The method of claim 73, wherein said patient has been diagnosed with, or is at risk of developing, a condition selected from the group consisting of tissue rejection, organ rejection, arthritis, an infection, dermatoses, inflammatory bowel disease, and an autoimmune disease.

75. A method for inhibiting antigen presentation in a cell comprising administering to a cell in need thereof an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;
wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X^{11} , at each occurrence, is independently one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}_2-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{CH}(\text{OH})-\text{CH}_2-\text{NH}-$, $-\text{CH}=\text{CH}-$, $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$, provided that when B^{11} is N, then X^{11} is $-\text{C}(\text{O})-\text{NH}-$;

X^{12} is one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$;

R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R^{11} , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{CH}_2-\text{R}^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

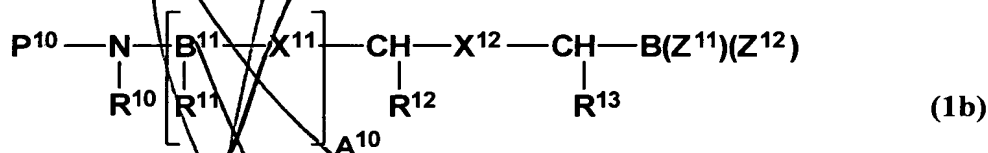
R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10-membered saturated, partially unsaturated or aromatic heterocycle or $-\text{CH}_2-\text{R}^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or -chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2.

76. A method for inhibiting inducible NF-κB dependent cell adhesion in an animal in need of said inhibiting, comprising administering to said animal an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;
wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

X¹¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided that when B¹¹ is N, then X¹¹ is -C(O)-NH;

X¹² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹¹ a nitrogen-containing

mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R^{11} , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

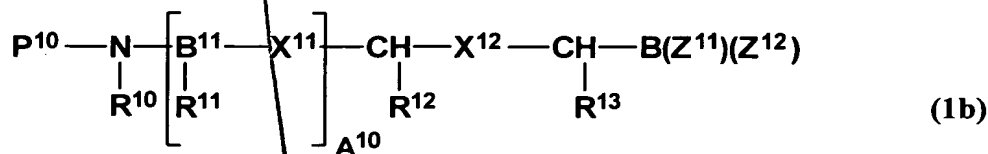
R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or $-chalcogen-alkyl$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A^{10} is 0, 1, or 2.

77. A method for inhibiting HIV replication in an animal in need of said inhibiting, comprising administering to said animal an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$,
5 $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH-NH_2$, $-CH=CH-$,
 $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided
that when B^{11} is N, then X^{11} is $-C(O)-NH$;

X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$,
10 $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or
when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing
mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14
ring members, that can be optionally substituted by one or two of keto, hydroxy,
alkyl, aryl, aralkyl, alkoxy or aryloxy;

15 R^{11} , at each occurrence, is independently one of hydrogen, alkyl,
cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic
heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl,
alkaryl or heterocycle can be optionally substituted;

20 R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl,
aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or
 $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

25 where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered
saturated, partially unsaturated or aromatic heterocycle, or
 $-chalcogen-alkyl$, where the ring portion of any of said aryl,
aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and
 Z^{12} together form a dihydroxy compound having at least two hydroxy groups
separated by at least two connecting atoms in a chain or ring, said chain or ring

comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2.

78. The method of claims 67, 68, 69, 70, 71, 72, 73, 75, 76 or 77 wherein said proteasome inhibitor is one of:

N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,
N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or
isosteres, pharmaceutically acceptable salts or boronate esters thereof.

79. A method for reducing the rate of muscle protein degradation in a cell comprising contacting said cell with a compound of claim 58 or 61.

80. A method for reducing the activity of NF-κB in a cell comprising contacting said cell with a compound of claim 58 or 61.

81. A method for reducing the rate of intracellular protein breakdown comprising contacting cells with a compound of claim 58 or 61.

82. A method for reducing the rate of degradation of p53 protein in a cell comprising administering to said cell a compound of claim 58 or 61.

83. A method for inhibiting cyclin degradation in a cell comprising contacting said cell with a compound of claim 58 or 61.

5 84. A method of preventing or treating an inflammatory condition in a patient in need thereof, said method comprising administering to said patient a compound of claim 58 or 61.

10 85. The method of claim 84, wherein said patient has been diagnosed with, or is at risk of developing, a condition selected from the group consisting of tissue rejection, organ rejection, arthritis, an infection, dermatoses, inflammatory bowel disease, asthma, osteoporosis, osteoarthritis and an autoimmune disease.

86. A method for inhibiting the growth of a cancer cell, comprising contacting said cell with a compound of claim 58 or 61.

87. A method for inhibiting antigen presentation in a cell comprising administering to said cell a compound of claim 58 or 61.

15 88. A method for inhibiting NF- κ B dependent cell adhesion in an animal comprising administering to said animal a compound of claim 58 or 61.

89. A method for inhibiting HIV replication in an animal comprising administering to said animal a compound of claim 58 or 61.